

## REMARKS

### I. Status of the Application

Claims 1-4, 7 and 8 are presently pending in the application. Applicants gratefully acknowledge the withdrawal of the rejection of claims 1-4, 7 and 8 under 35 U.S.C. §112, second paragraph, and the rejection of claims 1-4 and 7 under 35 U.S.C. §102 or 35 U.S.C. §103 over Huang et al. Claims 1-4 and 7 stand rejected under 35 U.S.C. §102(e) as being anticipated by or, in the alternative, under 35 U.S.C. §103(a) as being unpatentable over Hawker et al., U.S. Patent No. 6,413,587. Claims 1-4 and 7 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Hawker et al. and Mrksich et al. (1995) *TibTech* 13:228. Claims 1-4 and 7 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Huang et al. (1997) *Anal. Chem.* 69:4577, Hawker et al. and Mrksich et al. Claims 1-4, 7 and 8 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Hawker et al. and Mrksich et al., further in view of Mardare et al., U.S. Patent No. 5,312,871. Claims 1-4, 7 and 8 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Huang et al., Hawker et al., and Mrksich et al., further in view of Mardare et al. Applicants request entry and consideration of the foregoing remarks, which are intended to place this case in condition for allowance.

Applicants have amended the claims to more clearly define and distinctly characterize Applicants' novel invention. Specifically, claim 1 was amended to recite a "polynucleotide" array, and to recite covalently attaching a plurality of "polynucleotides" to a plurality of reactive groups on the polymeric brush, support for which can be found in the specification at least at page 34, Example 2, where Applicants teach the preparation of a polynucleotide array on polymeric brushes. Applicants respectfully submit that the amendments presented herein do not raise new issues requiring further search, and add no new matter.

## II. Claims 1-4 and 7 Are Novel and Nonobvious over Hawker

At page 3, section 5 of the instant Office Action, claims 1-4 and 7 stand rejected under §102(e) as being anticipated by Hawker et al. U.S. Patent No. 6,413,587, or under §103(a) as being unpatentable over Hawker et al. Applicants respectfully traverse this rejection in view of the amended claims now presented.

The pending claims are directed to method of preparing a polymeric brush substrate having a plurality of polynucleotides thereon for use in a *polynucleotide array*, the method comprising providing a substrate to which free radical initiators are covalently attached, wherein each free radical initiator has a radical generation site distal to the substrate, contacting the covalently attached substrate with monomers under conditions that promote free radical polymerization from the radical generation sites of the initiators to form a polymeric brush, and *covalently attaching a plurality of polynucleotides to a plurality of reactive groups on the polymeric brush*. Applicants have discovered a method by which polymeric brushes may be used to prepare polynucleotide arrays. Applicants' claimed polymeric brush substrate advantageously provides a much larger number of synthesis sites per unit area of substrate than was available using the monofunctional Silane-derivatized glass surfaces known at the time of filing (page 19, lines 10-12). Applicants' claimed polymeric brush substrate serves to substantially increase target binding to the array, thus enhancing detection as well as potentially providing kinetic enhancement (page 19, lines 13-15).

Hawker et al. fails to anticipate the claimed invention. Applicants respectfully submit that for a reference to anticipate a claim, the reference must teach every element of the claim. Hawker et al. does not teach or suggest *covalently attaching a plurality of polynucleotides to a plurality of reactive groups on a polymeric brush*, as claimed by Applicants. In fact, the

Examiner admits, at page 5 of the instant Office Action, that “Hawker et al. do not disclose covalently attaching a plurality of macromolecules to a plurality of reactive groups on the polymeric brush.” Accordingly, Hawker et al. fails to anticipate the claimed invention.

Applicants further submit that Hawker et al. fails to render the claimed invention obvious. Hawker et al. is directed to methods of making surfaces having a self-assembled monolayer and a polymer overlayer (abstract). Hawker et al. neither teaches nor suggests polymeric brushes for use in a polynucleotide array, nor does Hawker et al. teach or suggest covalently attaching a plurality of polynucleotides to a plurality of reactive groups on a polymeric brush. At most, Hawker et al. envisions brush polymers having an antigen or antibody bound thereto used to determine analyte binding, serving a function “analogous to a microparticle or titer plate,” and that their SAMs having brush polymers may serve as a high-density assay plates such as ELISA assay plates (column 12, lines 25-40 and lines 60-63). Nowhere does Hawker et al. teach or suggest binding a plurality of polynucleotides to a plurality of reactive groups on a polymeric brush. In fact, Hawker et al. fails to recognize that polymeric brushes may be useful for binding polynucleotides, let alone to suggest that polymeric brushes could be used as polynucleotide arrays.

Accordingly, Hawker et al. fails to teach or suggest all of Applicants’ claim limitations. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claims 1-4 and 7 under §102(b) or §103(a) as anticipated by or obvious over Hawker et al.

### III. Claims 1-4 and 7 Are Nonobvious over Hawker and Mrksich

At page 4, section 6 of the instant Office Action, claims 1-4 and 7 stand rejected under §103(a) as being unpatentable over Hawker et al. in view of Mrksich et al. (1995) *TibTech* 13:228. Applicants respectfully traverse this rejection.

Hawker et al. fails to teach or suggest the claimed invention for at least the reasons set forth above. Mrksich et al. fails to cure the deficiencies of Hawker et al. Mrksich et al. is directed to self-assembled monolayers (SAMs) made by microcontact printing. Mrksich et al. teaches several different methods for patterning SAMs (page 230, right column, page 231 left column). However, Mrksich et al. neither teaches nor suggests *polymeric brushes* or *covalently attaching a plurality of polynucleotides* to a plurality of reactive groups on a polymeric brush, as claimed by Applicants.

The Examiner is of the opinion that Mrksich et al. teaches attaching peptides and proteins to the organic surface of a SAM via SAM functional groups. The Examiner states that one of skill in the art would have had a reasonable expectation of success in covalently attaching a plurality of the peptides or antibodies to the polymeric brush because Mrksich et al. teach functional groups on a SAM for reacting with proteins and because Mrksich et al. teach the attachment of proteins to a SAM using photolithographic methods. The Examiner asserts that a SAM is “considered here to include a polymeric brush.” Applicants respectfully disagree with the Examiner’s assertion. A SAM is not equivalent to polymeric brush. Hawker et al. recognizes this, and teaches that SAMs have different physical properties than polymer brushes (column 1, line 37 to column 2, line 4).

Polymeric brushes add an additional dimension to SAMs. That is, while SAMs are a flat surface with attached polymers each having a *single*, terminal functional group at the surface

distal end which is easily accessible to added substrate (see, e.g., Mrksich et al. Figure 1a), polymer brushes are polymers having *many* functional groups *at many* sites on the polymer which can bind to many molecules (e.g., polynucleotides) (see, e.g., Figure 1C of the instant specification). One of skill in the art would have no reason to believe that the methods of adding a *protein* to a polymer having a *single* functional group, as taught by Mrksich et al., could be used to covalently attach *polynucleotides* to *a plurality of functional groups* on a polymeric brush with a reasonable expectation of success. For example, due to the physical properties of the polymeric brushes, one of skill in the art could not just assume that the plurality of functional groups would be accessible to a polynucleotide using the methods of Mrksich, or that a polymeric brush would be suitable for use as a polynucleotide array. It is only Applicants' disclosure which teaches that the claimed method produces a polymeric brush substrate suitable for such use.

Accordingly, the combination of Hawker et al. and Mrksich et al. fails to teach or suggest Applicants' claimed invention. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claims 1-4 and 7 under §103(a) as obvious over Hawker et al. in view of Mrksich et al.

#### **IV. Claims 1-4, 7 and 8 Are Nonobvious over Hawker and Mrksich in View of Mardare**

At page 10, section 8 of the instant Office Action, claims 1-4, 7 and 8 stand rejected under §103(a) as being unpatentable over Hawker et al. and Mrksich et al. further in view of Mardare et al., U.S. Patent No. 5,312,871. Applicants respectfully traverse this rejection.

The combination of Hawker et al. and Mrksich et al. fails to teach or suggest the claimed invention for at least the reasons set forth above. Mardare et al. fails to cure the deficiencies of

the primary references. Mardare et al. is directed to a method for living free radical polymerization (column 1, lines 6-9). Mardare et al. teaches a variety of methods whereby living free radical polymerization is carried out *in solution*. Mardare et al. neither teaches nor suggests covalently attaching a plurality of polynucleotides to a plurality of reactive groups on a polymeric brush as claimed by Applicants.

Accordingly, the combination of Hawker et al., Mrksich et al. and Mardare et al. fails to teach or suggest Applicants' claimed invention. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claims 1-4, 7 and 8 under §103(a) as obvious over Hawker et al. and Mrksich et al., further in view of Mardare et al.

**V. Claims 1-4 and 7 Are Nonobvious over Huang, Hawker and Mrksich**

At page 7, section 7 of the instant Office Action, claims 1-4 and 7 stand rejected under §103(a) as being unpatentable over Huang et al. (1997) Anal. Chem. 69:4577, Hawker et al. and Mrksich et al. Applicants respectfully traverse this rejection.

Huang et al. is directed to the growth of thin polymer films on silica (abstract). Huang et al. teaches that such films are useful for nonlinear optical materials, microfabrication, biocompatible medical implants and capillaries for electrophoresis (page 4577, first paragraph). Huang et al. neither teaches nor suggests the use of their films as polynucleotide arrays, nor does Huang et al. teach or suggest covalently attaching a *plurality of polynucleotides to a plurality of reactive groups* on a polymeric brush as claimed by Applicants. Although the Examiner is of the opinion that the thin film of Huang et al. reads on Applicants' claimed polymeric brush, the Examiner admits that Huang et al. *does not disclose* covalently attaching a plurality of macromolecules to a plurality of reactive groups on a polymeric brush.

Hawker et al. and Mrksich et al. fail to cure the deficiencies of Huang et al. As discussed above, the combination of Hawker et al. and Mrksich et al. fail to teach or suggest attaching a plurality of polynucleotides to a plurality of reactive groups on a polymeric brush. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claims 1-4 and 7 under §103(a) as obvious over Huang et al., Hawker et al. and Mrksich et al.

**VI. Claims 1-4, 7 and 8 Are Nonobvious over Huang, Hawker and Mrksich in View of Mardare**

At page 11, section 9 of the instant Office Action, claims 1-4, 7 and 8 stand rejected under §103(a) as being unpatentable over Huang et al., Hawker et al. and Mrksich et al., further in view of Mardare et al. Applicants respectfully traverse this rejection.

The combination of Huang et al., Hawker et al. and Mrksich et al. fails to teach or suggest the claimed invention for at least the reasons set forth above. Mardare et al. fails to cure the deficiencies of the primary references. Mardare et al. is directed to a method for living free radical polymerization (column 1, lines 6-9). Mardare et al. teaches a variety of methods whereby living free radical polymerization is carried out in solution. Mardare et al. neither teaches nor suggests covalently attaching a plurality of polynucleotides to a plurality of reactive groups on a polymeric brush as claimed by Applicants.

Accordingly, the combination of Huang et al., Hawker et al., Mrksich et al. and Mardare et al. fails to teach or suggest Applicants' claimed invention. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claims 1-4, 7 and 8 under §103(a) as obvious over Huang et al., Hawker et al. and Mrksich et al., further in view of Mardare et al.

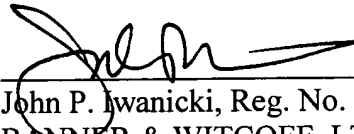
**VII. Conclusion**

Having addressed all outstanding issues, Applicants respectfully request reconsideration and allowance of all pending claims. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is requested to telephone the undersigned at the number below.

Respectfully submitted,

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